

## Message

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**From:** Lavoie, Emma [Lavoie.Emma@epa.gov]  
**Sent:** 1/25/2018 11:18:34 PM  
**To:** Bahadori, Tina [Bahadori.Tina@epa.gov]  
**Subject:** Fwd: PKWG Follow-up for Mn

I told mike to send as he doesn't work on Friday's.  
See below.

Emma

Begin forwarded message:

**From:** "Wright, Michael" <Wright.Michael@epa.gov>  
**Date:** January 25, 2018 at 5:51:13 PM EST  
**To:** "Schlosser, Paul" <Schlosser.Paul@epa.gov>, "Boyes, William" <Boyes.William@epa.gov>, "Kenyon, Elaina" <Kenyon.Elaina@epa.gov>, "Sasso, Alan" <Sasso.Alan@epa.gov>, "Lin, Yu-Sheng" <Lin.Yu-Sheng@epa.gov>, "White, Paul" <White.Paul@epa.gov>, "Jarabek, Annie" <Jarabek.Annie@epa.gov>, "Morozov, Viktor" <Morozov.Viktor@epa.gov>  
**Cc:** "Kopylev, Leonid" <Kopylev.Leonid@epa.gov>, "Brown, James" <Brown.James@epa.gov>, "Bateson, Thomas" <Bateson.Thomas@epa.gov>, "Lavoie, Emma" <Lavoie.Emma@epa.gov>, "Gigot, Carolyn" <gigot.carolyn@epa.gov>, "Bussard, David" <Bussard.David@epa.gov>, "jmikewright@yahoo.com" <jmikewright@yahoo.com>  
**Subject:** PKWG Follow-up for Mn

Dear PKWG members:

We really appreciate the time you have spent deliberating the issues related to the PK Models noted in Appendix B especially given our tight deadline for this project. As noted in the initial request from December, I wanted to reiterate what the expected scope and charge to the PKWG was.  
Here's the original Charge:

**The Purpose of the Initial PKWG Scoping Session** is to: identify a review process for the document entitled "*IRIS Assessment Plan for Manganese (Inhalation) - Appendix B: Consideration of Pharmacokinetic Models*". Appendix B supports the Mn team's determination that the two available PK models do not sufficiently inform the exposure-response relationship, derived from multiple, well-conducted epidemiology studies, to warrant use in calculating an exposure-dose-response relationship for humans exposed predominantly to inhaled manganese oxides. Although not the subject of the PKWG review, the evaluation of particle dosimetry that will be incorporated into the assessment is provided for context.

In addition to providing specific comments on the Appendix B, we welcome thoughts on the following questions.

# Ex. 5 Deliberative Process (DP)

We also recognize the challenges of trying to develop a consensus document, so we are at least hoping that the key scientific issues identified by the PKWG members are individually captured and sent to us. A short summary report from the PKWG effort would also be welcome, but please do not hold up the individual sets of comments for the report.

We would like comments on Appendix B provided by next Friday (2/2/18). If that creates a hardship for any of you, please let me know. Tomorrow is my CWD, but please don't hesitate to contact us with any further questions.

Thanks again for the assistance!  
Mike

J. Michael Wright, ScD  
U.S. Environmental Protection Agency  
National Center for Environmental Assessment  
26 W. Martin Luther King Drive (MS-A110)  
Cincinnati, OH 45268  
513 569 7922 (phone)  
513 487 2539 (fax)

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**From:** Schlosser, Paul  
**Sent:** Thursday, January 11, 2018 9:54 AM  
**To:** Boyes, William <Boyes.William@epa.gov>; Kenyon, Elaina <Kenyon.Elaina@epa.gov>; Sasso, Alan <Sasso.Alan@epa.gov>; Lin, Yu-Sheng <Lin.Yu-Sheng@epa.gov>; White, Paul <White.Paul@epa.gov>; Jarabek, Annie <Jarabek.Annie@epa.gov>; Morozov, Viktor <Morozov.Viktor@epa.gov>  
**Cc:** Kopylev, Leonid <Kopylev.Leonid@epa.gov>; Wright, Michael <Wright.Michael@epa.gov>; Brown, James <Brown.James@epa.gov>; Bateson, Thomas <Bateson.Thomas@epa.gov>; Lavoie, Emma <Lavoie.Emma@epa.gov>; Gigot, Carolyn <gigot.carolyn@epa.gov>  
**Subject:** RE: New call-in #: 202-991-0477, # 8831795

P.S. I should have cut down on the 'to' list for the last email, am doing so now.

I will look at these materials on other model components more carefully when I can... may not be until a couple of weeks from now.

But it's going to take a lot to convince me that 7 fitted parameters are needed to describe the brain tissue concentration when there are only 4 exposure levels/concentrations in the data set (what's shown in Fig. 9 of Schroeter et al., 2011, and that I see in Nong et al., 2009).

-Paul

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**From:** Boyes, William  
**Sent:** Wednesday, January 10, 2018 5:09 PM  
**To:** Schlosser, Paul <Schlosser.Paul@epa.gov>; Kenyon, Elaina <Kenyon.Elaina@epa.gov>; El-Masri, Hisham <El-Masri.Hisham@epa.gov>; Simmons, Jane <Simmons.Jane@epa.gov>; Lipscomb, John <lipscomb.john@epa.gov>; Sasso, Alan <Sasso.Alan@epa.gov>; Brinkerhoff, Chris <Brinkerhoff.Chris@epa.gov>; Lin, Yu-Sheng <Lin.Yu-Sheng@epa.gov>; White, Paul <White.Paul@epa.gov>; Tan, Cecilia <Tan.Cecilia@epa.gov>; Jarabek, Annie <Jarabek.Annie@epa.gov>; Morozov, Viktor <Morozov.Viktor@epa.gov>; IRIS Calendar <IRIS\_Calendar@epa.gov>; Kapraun, Dustin <Kapraun.Dustin@epa.gov>  
**Cc:** Kopylev, Leonid <Kopylev.Leonid@epa.gov>; Wright, Michael <Wright.Michael@epa.gov>; Brown,

James <[Brown.James@epa.gov](mailto:Brown.James@epa.gov)>; Bateson, Thomas <[Bateson.Thomas@epa.gov](mailto:Bateson.Thomas@epa.gov)>; Lavoie, Emma <[Lavoie.Emma@epa.gov](mailto:Lavoie.Emma@epa.gov)>; Gigot, Carolyn <[gigot.carolyn@epa.gov](mailto:gigot.carolyn@epa.gov)>

**Subject:** RE: New call-in #: 202-991-0477, # 8831795

Hi All

I have attached a prepublication copy of Nong et al., shared with EPA prior to publication, which contains in supplemental materials a description of the basis for setting many of the parameters in the rat and monkey PBPK models. I have also attached a memo from Nong and Anderson responding to EPA's request for further clarification of the basis for parameter settings. Finally I am including a prepublication copy of Dorman et al 2006(b) that shows clearance of manganese from tissues of monkeys after termination of 60 days exposure.

Among the points to note:

## Ex. 5 Deliberative Process (DP)

Will

-----Original Appointment-----

**From:** Schlosser, Paul

**Sent:** Wednesday, December 20, 2017 10:38 AM

**To:** Schlosser, Paul; Kenyon, Elaina; El-Masri, Hisham; Simmons, Jane; Lipscomb, John; Sasso, Alan; Brinkerhoff, Chris; Lin, Yu-Sheng; White, Paul; Tan, Cecilia; Jarabek, Annie; Morozov, Viktor; IRIS Calendar; Kapraun, Dustin

**Cc:** Kopylev, Leonid; Wright, Michael; Brown, James; Boyes, William; Bateson, Thomas; Lavoie, Emma; Gigot, Carolyn

**Subject:** New call-in #: 202-991-0477, # 8831795

**When:** Wednesday, January 10, 2018 12:00 PM-1:00 PM (UTC-05:00) Eastern Time (US & Canada).

**Where:** RTP-B230-Max20-NCEA/RTP-Bldg-B

**Note new call-in information!**

I'm also attaching a review article that Will sent. This linked article may also be of interest:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3965573/pdf/nihms561430.pdf>

[Added RTP room B-230 and tentative call-in (will update if that's not available).

Notes from other invitation copied below and same files added here.]

\*\* I'm shifting the time for this meeting to accommodate Annie Jarabek's schedule. Meeting room for RTP is now B-230.

-Paul

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For our January 10 meeting, and a preceding discussion that I'll set up for January 8, we will discuss a draft scoping for manganese PBPK modeling. A majority on this list have been included in separate emails, but this announcement assures that all are aware.

\*\* If you have *\*not\** been on the separate emails but would like to participate or listen in on January 8, please let me know.

I am attaching three documents:

- 1) <!--[if !supportLists]--><![endif]-->**PKWG-Preparing for a Scoping Session\_Mn.doc**, that provides some general background information and context
- 2) <!--[if !supportLists]--><![endif]-->**Mn ScopingEvaluation v5 Tox Sci.docx**, prepared for us in 2013 by Battelle, provides a descriptive review of the development of the models, including a figure that shows the relationship and flow among the modeling papers.
- 3) <!--[if !supportLists]--><![endif]-->**Mn PK issues 120817.docx**, which is a critical evaluation of the modeling and its potential for current application

Ex. 5 Deliberative Process (DP)

## **Ex. 5 Deliberative Process (DP)**

## **Ex. 5 Deliberative Process (DP)**

## **Ex. 6 Personal Privacy (PP)**

Other papers should be on HERO.

-Paul